immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome

Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome is characterized by the development of multiple autoimmune disorders in affected individuals. Autoimmune disorders occur when the immune system malfunctions and attacks the body's own tissues and organs. Although IPEX syndrome can affect many different areas of the body, autoimmune disorders involving the intestines, skin, and hormone-producing (endocrine) glands occur most often. Most patients with IPEX syndrome are males, and the disease can be life-threatening in early childhood.

Almost all individuals with IPEX syndrome develop a disorder of the intestines called enteropathy. Enteropathy occurs when certain cells in the intestines are destroyed by a person's immune system. It causes severe diarrhea, which is usually the first symptom of IPEX syndrome. Enteropathy typically begins in the first few months of life. It can cause failure to gain weight and grow at the expected rate (failure to thrive) and general wasting and weight loss (cachexia).

People with IPEX syndrome frequently develop inflammation of the skin, called dermatitis. Eczema is the most common type of dermatitis that occurs in this syndrome, and it causes abnormal patches of red, irritated skin. Other skin disorders that cause similar symptoms are sometimes present in IPEX syndrome.

The term polyendocrinopathy is used in IPEX syndrome because individuals can develop multiple disorders of the endocrine glands. Type 1 diabetes mellitus is an autoimmune condition involving the pancreas and is the most common endocrine disorder present in people with IPEX syndrome. It usually develops within the first few months of life and prevents the body from properly controlling the amount of sugar in the blood. Autoimmune thyroid disease may also develop in people with IPEX syndrome. The thyroid gland is a butterfly-shaped organ in the lower neck that produces hormones. This gland is commonly underactive (hypothyroidism) in individuals with this disorder, but may become overactive (hyperthyroidism).

Individuals with IPEX syndrome typically develop other types of autoimmune disorders in addition to those that involve the intestines, skin, and endocrine glands. Autoimmune blood disorders are common; about half of affected individuals have low levels of red blood cells (anemia), platelets (thrombocytopenia), or white blood cells (neutropenia) because these cells are attacked by the immune system. In some individuals, IPEX syndrome involves the liver and kidneys.

Frequency

IPEX syndrome is a rare disorder; its prevalence is unknown.

Genetic Changes

Mutations in the *FOXP3* gene cause some cases of IPEX syndrome. The protein produced from this gene is a transcription factor, which means that it attaches (binds) to specific regions of DNA and helps control the activity of particular genes. This protein is essential for the production and normal function of certain immune cells called regulatory T cells. Regulatory T cells play an important role in controlling the immune system and preventing autoimmune disorders. Mutations in the *FOXP3* gene lead to reduced numbers or a complete absence of regulatory T cells. Without the proper number of regulatory T cells, the body cannot control immune responses. Normal body tissues and organs are attacked, causing the multiple autoimmune disorders present in people with IPEX syndrome.

About half of individuals diagnosed with IPEX syndrome do not have identified mutations in the *FOXP3* gene. In these cases, the cause of the disorder is unknown.

Inheritance Pattern

When IPEX syndrome is due to mutations in the *FOXP3* gene, it is inherited in an X-linked recessive pattern. The *FOXP3* gene is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation must be present in both copies of the gene to cause the disorder. Males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Some people have a condition that appears identical to IPEX syndrome, but they do not have mutations in the *FOXP3* gene. The inheritance pattern for this IPEX-like syndrome is unknown, but females can be affected.

Other Names for This Condition

- insulin-dependent diabetes mellitus secretory diarrhea syndrome
- IPEX syndrome

Diagnosis & Management

These resources address the diagnosis or management of IPEX syndrome:

- GeneReview: IPEX Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1118
- Genetic Testing Registry: Insulin-dependent diabetes mellitus secretory diarrhea syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0342288/
- Seattle Children's Hospital
  http://www.seattlechildrens.org/healthcare-professionals/access-services/diagnostic-services/laboratories/immunology-diagnostic-laboratory/disorders/ipex/

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Type 1 Diabetes
  https://medlineplus.gov/ency/article/000305.htm
- Health Topic: Autoimmune Diseases
  https://medlineplus.gov/autoimmunediseases.html
- Health Topic: Immune System and Disorders
  https://medlineplus.gov/immunesystemanddisorders.html

Genetic and Rare Diseases Information Center

- Immunodysregulation, polyendocrinopathy and enteropathy X-linked
  https://rarediseases.info.nih.gov/diseases/1850/immunodysregulation-polyendocrinopathy-and-enteropathy-x-linked

Additional NIH Resources

- National Institute of Diabetes and Digestive and Kidney Diseases: Hyperthyroidism
  https://www.niddk.nih.gov/health-information/health-topics/endocrine/primary-hyperparathyroidism/Pages/fact-sheet.aspx
- National Institute of Diabetes and Digestive and Kidney Diseases: Hypothyroidism
  https://www.niddk.nih.gov/health-information/health-topics/endocrine/hypothyroidism/Pages/fact-sheet.aspx
- National Institute of Diabetes and Digestive and Kidney Diseases: Monogenic Forms of Diabetes
  https://www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes/monogenic-neonatal-mellitus-mody

Educational Resources

- Boston Children's Hospital: Autoimmune Diseases
  http://www.childrenshospital.org/conditions-and-treatments/conditions/a/autoimmune-diseases
- Disease InfoSearch: Insulin-dependent diabetes mellitus secretory diarrhea syndrome
  http://www.diseaseinfosearch.org/Insulin-dependent+diabetes+mellitus+secretory+diarrhea+syndrome/8674
- Immune Deficiency Foundation: Patient and Family Handbook for Primary Immunodeficiency Diseases
  http://primaryimmune.org/patient-family-handbook/
- Kids Health: Eczema
  http://kidshealth.org/en/parents/eczema-atopic-dermatitis.html
- Kids Health: Type 1 Diabetes
  http://kidshealth.org/en/parents/type1.html
- MalaCards: immune dysregulation, polyendocrinopathy, enteropathy, x-linked syndrome
  http://www.malacards.org/card/immune_dysregulation_polyendocrinopathy_enteropathy_x_linked_syndrome
- Merck Manual Professional Version: Polyglandular Deficiency Syndromes
  http://www.merckmanuals.com/professional/endocrine-and-metabolic-disorders/polyglandular-deficiency-syndromes/polyglandular-deficiency-syndromes
- Orphanet: Immune dysregulation-polyendocrinopathy-enteropathy-X-linked syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=37042

Patient Support and Advocacy Resources

- Immune Deficiency Foundation
  http://primaryimmune.org/
- International Patient Organisation for Patients with Primary Immunodeficiencies
  http://ipopi.org/
- Jeffrey Modell Foundation: National Primary Immunodeficiency Resource Center
  http://www.info4pi.org

GeneReviews

- IPEX Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1118

Genetic Testing Registry

- Insulin-dependent diabetes mellitus secretory diarrhea syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0342288/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22immune+dysregulation%2C+polyendocrinopathy%2C+enteropathy%2C+X-linked+syndrome%22

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28immune+dysregulation+polyendocrinopathy+enteropathy+x-linked%29+OR+%28IPEX%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- IMMUNODYSREGULATION, POLYENDOCRINOPATHY, AND ENTEROPATHY, X-LINKED
  http://omim.org/entry/304790

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https://ghr.nlm.nih.gov/condition/immune-dysregulation-polyendocrinopathy-enteropathy-x-linked-syndrome

Reviewed: January 2014
Published: January 24, 2017

Lister Hill National Center for Biomedical Communications
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National Institutes of Health
Department of Health & Human Services